

CLAIMS

1. A chimeric antigen receptor (CAR) specific for at least one IL-23 receptor (IL-23R), wherein said CAR comprises:
 - (i) an extracellular binding domain, wherein said binding domain binds to said IL-23R,
 - (ii) optionally an extracellular hinge domain,
 - (iii) a transmembrane domain,
 - (iv) an intracellular signaling domain, and,
 - (v) optionally a tag and/or a leader sequence.
2. The CAR according to claim 1, wherein the extracellular binding domain comprises a scFv fragment directed against said IL-23R.
3. The CAR according to claim 1 or claim 2, wherein the extracellular binding domain comprises a scFv fragment directed against said IL-23R, wherein said scFv comprises a heavy chain variable domain (VH) and a light chain variable domain (VL) and optionally a linker between the VH and the VL, wherein

the heavy chain variable domain (VH) has the sequence of SEQ ID NO: 37, and

the light chain variable domain (VL) has a sequence selected from the group consisting of SEQ ID NOs: 38, 46 and 56,

preferably wherein said scFv has the sequence SEQ ID NO: 55.
4. The CAR according to any one of claims 1 to 3, wherein the hinge domain is a hinge region of human CD8, preferably having the sequence of SEQ ID NO: 13.
5. The CAR according to any one of claims 1 to 4, wherein the transmembrane domain is a transmembrane domain derived from the human CD8 α , preferably having the sequence of SEQ ID NO: 21.

6. The CAR according to any one of claims 1 to 5, wherein the intracellular signaling domain comprises a costimulatory signaling domain of a molecule selected from the group consisting of 4-1BB, ICOS, CD27, OX40, CD28, CTLA4 and PD-1 and a T cell primary signaling human CD3 zeta.
7. The CAR according to any one of claims 1 to 6, wherein the intracellular signaling domain comprises a costimulatory signaling domain of human 4-1BB having the sequence of SEQ ID NO: 29 and a T cell primary signaling human CD3 zeta having the sequence of SEQ ID NO: 26.
8. The CAR according to any one of claims 1 to 7, wherein the intracellular signaling domain comprises a costimulatory signaling domain of CD28 having the sequence of SEQ ID NO: 31 and a T cell primary signaling human CD3 zeta having the sequence of SEQ ID NO: 26.
9. The CAR according to any one of claims 1 to 8, comprising
 - (i) an anti-IL-23R scFv, preferably comprising a VH and a VL, preferably wherein the VH has the sequence of SEQ ID NO: 37 and wherein the VL has the sequence of SEQ ID NO: 38, linked by a (G4S)₃ linker (SEQ ID NO: 3),
 - (ii) a hinge domain derived from CD8 α , preferably having the sequence SEQ ID NO: 13,
 - (iii) a human CD8 α transmembrane domain, preferably having the sequence SEQ ID NO: 21,
 - (iv) an intracellular signaling domain comprising a costimulatory signaling domain of a molecule selected from the group consisting of 4-1BB, ICOS, CD27, OX40, CTLA4 and PD-1, preferably a costimulatory signaling domain of human 4-1BB having the sequence SEQ ID NO: 29 or of CD28 having the sequence SEQ ID NO: 31, and a human CD3 zeta domain, preferably having the sequence SEQ ID NO: 26, and
 - (v) optionally a tag and/or a leader sequence.
10. A nucleic acid sequence encoding a CAR according to any one of claims 1 to 9.
11. A vector comprising the nucleic acid sequence according to claim 10.

12. A T cell population, engineered to express on the cell surface a CAR according to any one of claims 1 to 9.
13. The T cell population according to claim 12, wherein said T cell population is a regulatory T cell population, preferably wherein said regulatory T cell population is selected from the group consisting of CD4⁺CD25⁺Foxp3⁺ Treg, Tr1 cells, TGF- β secreting Th3 cells, regulatory NKT cells, regulatory $\gamma\delta$ T cells, regulatory CD8⁺ T cells, and double negative regulatory T cells.
14. A composition comprising at least one T cell population engineered to express on the cell surface a CAR according to any one of claims 1 to 9, wherein said composition is preferably a pharmaceutical composition further comprising at least one pharmaceutically acceptable excipient or carrier.
15. An *ex vivo* method for obtaining a T cell population engineered to express on the cell surface a CAR according to any one of claims 1 to 9, wherein said *ex vivo* method comprises the genetic modification, preferably the transduction, of at least one T cell with a nucleic acid encoding an IL-23R-CAR, and optionally an expansion step of the transduced cells.
16. Use of the T cell population according to claim 12 or 13, or the composition according to claim 14 for the manufacture of a medicament for the treatment of an IL-23R expressing cell-mediated disease or disorder in a subject in need thereof, wherein said IL-23R expressing cell-mediated disease or disorder is preferably an autoimmune and/or inflammatory disease and/or disorder.
17. Use according to claim 16, wherein said autoimmune and/or inflammatory disease and/or disorder is selected from the group consisting of inflammatory bowel diseases, systemic lupus erythematosus, rheumatoid arthritis, juvenile idiopathic arthritis, Sjögren syndrome, systemic sclerosis, ankylosing spondylitis, Type 1 diabetes, autoimmune thyroid disorders, multiple sclerosis, Myasthenia Gravis, psoriasis, psoriatic arthritis and uveitis, preferably wherein said autoimmune and/or inflammatory disease and/or disorder is Crohn's disease or ulcerative colitis.

CLAIMS

1. Use of a regulatory T cell population engineered to express on the cell surface a chimeric antigen receptor (CAR) specific for at least one IL-23 receptor (IL-23R) in the manufacture of a medicament for the treatment of an IL-23R expressing cell-mediated disease or disorder in a subject in need thereof,

wherein said IL-23R expressing cell-mediated disease or disorder is an autoimmune and/or inflammatory disease and/or disorder,

wherein said CAR comprises:

- (i) an extracellular binding domain, wherein said binding domain binds to said IL-23R,
- (ii) optionally an extracellular hinge domain,
- (iii) a transmembrane domain,
- (iv) an intracellular signaling domain comprising a costimulatory signaling domain of a molecule selected from the group consisting of 4-1BB, ICOS, CD27, OX40, CD28, CTLA4 and PD-1 and a T cell primary signaling human CD3 zeta, and,
- (v) optionally a tag and/or a leader sequence.

2. The use according to claim 1, wherein the extracellular binding domain of the CAR comprises a scFv fragment directed against said IL-23R.

3. The use according to claim 1 or claim 2, wherein the extracellular binding domain of the CAR comprises a scFv fragment directed against said IL-23R, wherein said scFv comprises a heavy chain variable domain (VH) and a light chain variable domain (VL) and optionally a linker between the VH and the VL, wherein

the heavy chain variable domain (VH) has the sequence of SEQ ID NO: 37, and

the light chain variable domain (VL) has a sequence selected from the group consisting of SEQ ID NOs: 38, 46 and 56,

preferably wherein said scFv has the sequence SEQ ID NO: 55.

4. The use according to any one of claims 1 to 3, wherein the hinge domain is a hinge region of human CD8, preferably having the sequence of SEQ ID NO: 13.
5. The use according to any one of claims 1 to 4, wherein the transmembrane domain of the CAR is a transmembrane domain derived from the human CD8 α , preferably having the sequence of SEQ ID NO: 21.
6. The use according to any one of claims 1 to 5, wherein:
 - a) the extracellular binding domain of the CAR comprises a scFv fragment directed against said IL-23R, wherein said scFv has the sequence SEQ ID NO: 55;
 - b) the transmembrane domain of the CAR is derived from the human CD8 α having the sequence of SEQ ID NO: 21;
 - c) the extracellular binding domain of the CAR comprises a scFv fragment directed against said IL-23R, wherein there is a linker between the VH and VL; and/or
 - d) the CAR comprises an extracellular hinge region.
7. The use according to claim 6, wherein the CAR comprises an extracellular hinge region and the hinge region of the CAR is a hinge region of human CD8 having the sequence of SEQ ID NO: 13.
8. The CAR according to any one of claims 1 to 7, wherein the intracellular signaling domain comprises a costimulatory signaling domain of human 4-1BB having the sequence of SEQ ID NO: 29 and a T cell primary signaling human CD3 zeta having the sequence of SEQ ID NO: 26.
9. The CAR according to any one of claims 1 to 8, wherein the intracellular signaling domain comprises a costimulatory signaling domain of CD28 having the sequence of SEQ ID NO: 31 and a T cell primary signaling human CD3 zeta having the sequence of SEQ ID NO: 26.

10. The use according to any one of claims 1 to 9, wherein the CAR comprises
 - (i) an anti-IL-23R scFv, preferably comprising a VH and a VL, preferably wherein the VH has the sequence of SEQ ID NO: 37 and wherein the VL has the sequence of SEQ ID NO: 38, linked by a (G₄S)₃ linker (SEQ ID NO: 3),
 - (ii) a hinge domain derived from CD8 α , preferably having the sequence SEQ ID NO: 13,
 - (iii) a human CD8 α transmembrane domain, preferably having the sequence SEQ ID NO: 21,
 - (iv) an intracellular signaling domain comprising a costimulatory signaling domain of a molecule selected from the group consisting of 4-1BB, ICOS, CD27, OX40, CTLA4 and PD-1, preferably a costimulatory signaling domain of human 4-1BB having the sequence SEQ ID NO: 29 or of CD28 having the sequence SEQ ID NO: 31, and a human CD3 zeta domain, preferably having the sequence SEQ ID NO: 26, and
 - (v) optionally a tag and/or a leader sequence.
11. The use according to claim 10, wherein the CAR comprises:
 - a) an anti-IL-23R scFv, comprising a VH and a VL, wherein the VH has the sequence of SEQ ID NO: 37 and wherein the VL has the sequence of SEQ ID NO: 38, linked by a (G₄S)₃ linker (SEQ ID NO: 3);
 - b) a hinge domain derived from CD8 α , having the sequence SEQ ID NO: 13;
 - c) a human CD8 α transmembrane domain, having the sequence SEQ ID NO: 21;
 - d) an intracellular signaling domain comprising costimulatory signaling domain of human 4-1BB having the sequence SEQ ID NO: 29, or comprising costimulatory signaling domain of CD28 having the sequence SEQ ID NO: 31;
 - e) an intracellular signaling domain comprising a human CD3 zeta domain, having the sequence SEQ ID NO: 26; and/or
 - f) a tag and/or a leader sequence.

12. The use according to any one of claims 1 to 11, wherein said T cell population is a regulatory T cell population.
13. The use according to claim 12, wherein said regulatory T cell population is selected from the group consisting of CD4⁺CD25⁺Foxp3⁺ Treg, Tr1 cells, TGF- β secreting Th3 cells, regulatory NKT cells, regulatory $\gamma\delta$ T cells, regulatory CD8⁺ T cells, and double negative regulatory T cells.
14. The use according to any one of claims 1 to 13, wherein said autoimmune and/or inflammatory disease and/or disorder is selected from the group consisting of inflammatory bowel diseases, systemic lupus erythematosus, rheumatoid arthritis, juvenile idiopathic arthritis, Sjögren syndrome, systemic sclerosis, ankylosing spondylitis, Type 1 diabetes, autoimmune thyroid disorders, multiple sclerosis, Myasthenia Gravis, psoriasis, psoriatic arthritis and uveitis, preferably wherein said autoimmune and/or inflammatory disease and/or disorder is Crohn's disease or ulcerative colitis.
15. An *in vitro* regulatory T cell population engineered to express on the cell surface a chimeric antigen receptor (CAR) specific for at least one IL-23 receptor (IL-23R), wherein said CAR comprises:
 - (i) an extracellular binding domain, wherein said binding domain binds to said IL-23R,
 - (ii) optionally an extracellular hinge domain,
 - (iii) a transmembrane domain,
 - (iv) an intracellular signaling domain comprising a costimulatory signaling domain of a molecule selected from the group consisting of 4-1BB, ICOS, CD27, OX40, CD28, CTLA4 and PD-1 and a T cell primary signaling human CD3 zeta, and,
 - (v) optionally a tag and/or a leader sequence.
16. The regulatory T cell population of claim 16, wherein the CAR comprises an extracellular hinge domain.

17. The regulatory T cell population of claim 15 or 16, wherein the CAR comprises a tag and/or a leader sequence.